August 5, 2003

Thomas M. Gray, M.S., D.A.B.T.
Senior Toxicologist
The American Petroleum Institute
Petroleum HPV Testing Group
1220 L. Street, NW
Washington, DC 20005

Dear Dr. Gray:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Lubricating Oil Basestocks Category posted on the ChemRTK HPV Challenge Program Web site on April 4, 2003. I commend The American Petroleum Institute Petroleum HPV Testing Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The American Petroleum Institute Petroleum HPV Testing Group advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Lubricating Oil Basestocks

Summary of EPA Comments

The sponsor, the American Petroleum Institute, submitted a test plan and robust summaries to EPA for Lubricating Oil Basestocks dated March 24, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on April 4, 2003. The category consists of 36 substances subdivided into three subcategories: (1) unrefined and mildly refined distillate base oils, (2) highly and severely refined distillate base oils, and (3) residual base oils.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. Overall, the physicochemical and environmental fate properties of the lubricating oil basestocks support the category, but the available information on health or ecological effects does not.

2. Physicochemical Properties. The submitter needs to explain how representative data for all the physicochemical endpoints will be used to address data gaps for the remaining members of the category. Also, the submitter needs to address inconsistencies in the melting point values provided in the test plan, to provide vapor pressure data for more representative substances within the category, and to provide in robust summary format the results of its estimations for partition coefficient and water solubility.

3. Environmental Fate. The stability in water information provided by the submitter is adequate for the purposes of the HPV Challenge Program. The submitter needs to explain how representative data for photodegradation, biodegradation, and transport and distribution (fugacity) will be used to address data gaps for the remaining members of the category.

4. Health Effects. EPA agrees with the submitter's plan to test residual base oils and highly and severely refined distillate base oils subcategories for the reproductive/developmental endpoints. However, EPA recommends conducting these tests via the oral route instead of the proposed dermal route. EPA also recommends genetic toxicity studies and a combined repeated-dose/reproductive/developmental toxicity screening test for the category on unrefined and mildly refined distillate base oils subcategory. In addition, the submitter needs to address deficiencies in the robust summaries.

5. Ecological Effects. The data for the highly and severely refined distillate base oils subcategory in fish, aquatic invertebrates, and aquatic plants are adequate for the purposes of the HPV Challenge Program. However, no toxicity values or robust summaries were provided for the unrefined and mildly refined distillate base oils subcategory and only toxicity values (LL_0s) without robust summaries were submitted for acute fish and algae and chronic daphnia studies with residual base oils. Therefore, additional data on these two subcategories are needed to satisfy the ecological effects endpoints.

EPA Comments on the Lubricating Oil Basestocks Challenge Submission

Category Definition

The Lubricating Oil Basestocks Category consists of 36 petroleum process streams that are complex mixtures of paraffinic, isoparaffinic, naphthenic, and aromatic hydrocarbons in the C15-C50 range. The category is divided into three subcategories: 1) unrefined and mildly refined distillate base oils; 2) highly and severely refined distillate base oils; and 3) residual base oils. The residuum resulting from crude oil distillation at atmospheric pressure is the starting material for the lubricating oil basestocks category. This residuum is distilled under vacuum to yield a range of distillate fractions and a vacuum residuum. The distillate fractions undergo varying degrees of processing to produce streams of the unrefined and highly refined distillate base oil subcategories; removal of asphalt components and additional processing of the vacuum residuum results in streams of the residual base oils subcategory. The submitter also provided data on the analog heavy vacuum gas oil (CAS No. 64741-57-7), a material with a process history similar to that of the unrefined distillate base oils.

The names for two of the CAS numbers of category members provided in the test plan are inconsistent with the names listed in EPA's Substance Registry System (SRS) Data Base. According to SRS, CAS No. 64742-44-5 is described as "Distillates, petroleum, clay-treated heavy naphthenic" and CAS No. 72623-84-8 is described as "Lubricating oils, petroleum, C15-30, hydrotreated neutral oil-based, containing solvent deasphalted residual oil."

CAS number definitions for petroleum streams typically reflect the last processing step rather than the entire process history. Therefore, such descriptions for petroleum streams are by definition incomplete.

The category definition is adequate.

Category Justification

The submitter justifies the grouping of the category members on the basis of production streams that originate from a single starting material, similar physicochemical and environmental properties, low aquatic toxicities, and predictable toxicity trends across the subcategories and their associated degree of processing.

Overall, the physicochemical and environmental fate properties show a pattern that is consistent with the molecular composition of the members and support the category. However, the submitter does not explain how the submitted experimental or estimated values will be used to address data gaps for the remaining members of the category.

The submitter states that the distillate base oils subcategories contain relatively low molecular weight hydrocarbons that are both biologically available and contain contaminants (e.g., polycyclic aromatic compounds, heteroatoms, and metals) with the potential to cause adverse health effects. Removing these undesirable components through additional refining is believed to also remove their biological activity. This forms a basis for the submitter's hypothesis that the more highly refined distillate streams are less toxic than the unrefined and mildly refined distillate streams. For residual base oils, the submitter states that the relatively high molecular weight components of these hydrocarbons are not biologically available, that there is no association between degree of refining and toxicity, and that all the residual base oils are expected to have low toxicities. Therefore, the submitter suggests that the pattern of toxicities is consistent and supports the category. Finally, the submitter states that the uniformly low aquatic toxicity of the category members also supports the category.

Although there appears to be a relationship between processing and predicted levels of toxicity among the three subcategories, the available data are insufficient to support the category on the basis of health effects. Additional data are needed for members of all three subcategories to test the hypothesis presented by the submitter that adverse human health effects are a function of the type and degree of chemical processing. Even for the acute toxicity endpoint where a trend of low toxicity appears to be established for each subcategory, these data provide little substantiation that the category members are toxicologically similar in the absence of data on comparative target organ effects.

Similarly, the available ecological effects data are insufficient to support the the category. A full data set is available only for highly and severely refined distillate base oils but data are almost entirely lacking for the unrefined and mildly refined distillate base oils and for residual base oils.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

For all the physicochemical endpoints, the submitter needs to indicate how data gaps for category members not discussed in the test plan will be addressed.

The data submitted for melting point and boiling point are adequate for the purposes of the HPV Challenge Program, provided the submitter adequately describes how the remaining data gaps will be addressed. The data submitted for vapor pressure, partition coefficient and water solubility are inadequate.

Melting point. The submitter needs to address an inconsistency in the measured values given in the test plan. There is a large difference in the pour point data given in Table 2 (page 10) for representative "unrefined" (+ 60°F or 16°C) and "severely refined" (-32.8°F or -36°C) distillate base oils.

Vapor pressure. The submitter states that using estimated vapor pressures derived for model C15 hydrocarbons and Dalton's law of partial pressures to calculate a total vapor pressure for a mixture of hydrocarbons, testing vapor pressure of these substances is not necessary because the estimated vapor pressures are below the testing threshold of $1x10^{-5}$ Pa. However, the one measured vapor pressure value provided is almost 20 times this value. In addition, the test substance contained predominantly hydrocarbons with a carbon number range of 20 to 50, which may not be representative of substances with higher vapor pressures (e.g., mixtures containing hydrocarbons with carbon numbers starting at C15). Consequently, the data provided are inadequate to address this endpoint. The submitter needs to provide data or estimates on enough chemicals to represent all category members. EPA reserves judgement on the adequacy of data for this endpoint until the submitter provides additional data.

Partition coefficient. The submitter reported a range of estimated values for several structures covering paraffinic, naphthenic, and aromatic C_{15} compounds in the test plan (page 19), but no robust summary. Also, no information was included on any of the C20-C50 streams. The submitter stated that the WSKOW v1.40 estimation method was used to estimate values, but did not identify the model compounds used. Furthermore, the submitter stated in the test plan that the lower limit value of 4.9 for the estimated partition coefficient of the C15 compounds is consistent with the value of >4 measured for lubricating oil basestocks. However, these measured data are not summarized in the test plan. The submitter needs to summarize relevant measured data and estimation methods, including structures used in the estimation and an explanation for not including C20-C50 streams, as well as to provide the results of each estimation in robust summary format.

Water solubility. The submitter did not provide measured or estimated data for this endpoint in robust summary format. In the test plan, the submitter indicated that "water solubility values of 0.003 to 0.63 mg/L have been calculated for representative C15 hydrocarbon components of lubricating base oils." The

submitter further states that the WSKOW v1.40 estimation method was used to derive the estimates. However, the submitter does not identify the representative C15 hydrocarbons used in the calculations. The submitter needs to summarize the estimation methods, including structures used in the estimation, and the results of each estimation, in robust summary format. Water solubility is expected to decrease with increasing molecular weight, but the submitter also needs to explain how estimates will be assigned to other category members.

Environmental Fate (photodegradation, stability in water, biodegradation, transport and distribution (fugacity).

Adequate data are available for stability in water. For the other environmental fate endpoints, the submitter needs to indicate how data gaps for category members not discussed in the test plan will be addressed.

Photodegradation. The submitter provided estimated photooxidation half-life values for representative C15 hydrocarbons in reactions with photochemically produced hydroxyl radicals in air. Citing these estimations, the submitter states that there are adequate data for this endpoint. However, the submitter did not provide information on the structures used in estimating the range of the half-life values given in the robust summary. Therefore, EPA could not verify the submitter's estimates. The submitter needs to provide information on the structures used in their estimations, and the results of each estimation in robust summary format. Furthermore, the submitter needs to account for the C20 - C50 compounds in these estimates.

Biodegradation. The submitted data are based on adequately conducted studies. However, the submitter needs to indicate how data gaps for the remaining category members will be addressed.

Transport and distribution (fugacity). Although EPA had previously recommended the use of EQC Level I, EPA now recommends the use of EQC level III, which provides a more rigorous level of analysis. The submitter provided fugacity modeling results obtained from the EQC Level I model for nine C15 hydrocarbons, but did not provide the input parameters used. The submitter needs to provide this information in the robust summaries. The submitter did not indicate in the test plan how data gaps for the remaining category members will be addressed, including the C20 - C50 streams.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for the category for acute toxicity for the purposes of the HPV Challenge Program. EPA agrees with the submitter's plan to test residual base oils and highly and severely refined distillate base oils for the reproductive/developmental endpoints following OECD TGs 422 and 421, respectively. However, EPA recommends conducting these tests by the oral route, the preferred exposure route for OECD guidelines, instead of the proposed dermal route. EPA also recommends that the submitter conduct genetic toxicity studies for the category following OECD TGs 471 and 473 and a combined repeated-dose/reproductive/developmental toxicity screening test following OECD TG 422 on unrefined and mildly refined distillate base oils subcategory. In addition, the submitter needs to address deficiencies in the robust summaries.

Repeated-dose toxicity. Unrefined distillate base oils: Sufficient detail was not provided in the robust summary for the submitted 90-day dermal study of heavy vacuum gas oil, an analog of this subcategory, to allow for an independent evaluation of study adequacy. Since OECD guidelines recommend the oral exposure route, the submitter needs to provide adequate justification for using data from a dermal study and the missing study details; otherwise, additional repeated-dose toxicity testing by the oral route may be needed.

Highly refined distillate base oils: Although the submitted 90-day oral data are adequate, the test substance, food grade white oils, is expected to be among the least toxic of the highly refined base oils. Therefore, these data do not adequately characterize the potential toxicity of the highly refined base oils subcategory, unless adequate additional justification is provided to support the use of food grade oil to represent this subcategory. Adequate data may exist from the submitted 4-week inhalation repeated-dose toxicity study; however, the submitter needs to provide the missing study details.

The submitted dermal data are not adequate because the studies used a 3-day-per-week dosing schedule and the summaries did not include adequate experimental detail.

Residual base oils: No data were submitted. EPA agrees with the proposed OECD TG 422 test, but recommends the oral route, the preferred exposure route according to OECD guidelines, unless the submitter can provide adequate justification for selecting the dermal route. The submitter also needs to specify the residual base oil to be tested for the proposed OECD TG 422 test. A conservative (potentially more toxic) residual base oil should be tested.

Genetic toxicity. The data submitted for gene mutations for the category are inadequate because only one strain (TA 98) was tested. The data provided from the secondary source were too limited to address the chromosomal aberration endpoint. Therefore, the submitter needs to conduct genetic toxicity studies on unrefined and mildly refined distillate base oils for the category following OECD TGs 471 and 473. A conservative (potentially more toxic) unrefined and mildly refined distillate base oil should be tested.

Reproductive/developmental toxicity. Unrefined distillate base oils: Sufficient detail was not provided for the submitted dermal developmental study of a heavy vacuum gas oil in the robust summary to allow for an independent evaluation of study adequacy. Also, the submitter did not provide a justification for using data from a dermal study. As discussed under repeated-dose toxicity, if the submitter cannot provide the missing details and the justification of using data from a dermal study, an oral OECD TG 422 (a combined repeated-dose/reproductive/developmental toxicity screening test) will be needed, and a conservative (potentially more toxic) member of the unrefined distillate base oils subcategory should be tested.

Highly refined distillate base oils: Inadequate data were provided for two one-generation reproductive toxicity studies of a base oil and one oral developmental study of a white oil because the two refined oils were used as solvent controls. Therefore, there was no negative control with which to compare results from the two treated groups. The submitter plans to conduct a dermal OECD TG 421 test. EPA agrees but recommends the oral exposure route, the preferred exposure route by OECD guidelines, unless the use of another exposure route is justified. A conservative (potentially more toxic) member of the highly refined distillate base oils should be tested.

Residual base oils: No data were submitted for this subcategory. EPA agrees with the proposed OECD TG 422 test but recommends the oral exposure route, as noted above, unless the use of another exposure route is justified. A conservative (potentially more toxic) residual base oil needs to be tested.

<u>Ecological Effects (fish, invertebrates, and algae)</u>.

Toxicity values presented without essential robust summary details were included in a "Remark" section within robust summaries for acute toxicity in fish, acute toxicity in algae, and chronic toxicity in daphnia. The reliability of those data cannot be independently evaluated and therefore cannot be used to satisfy these SIDS endpoints.

Fish. Adequate data are available for the highly refined distillate base oils subcategory. Adequate data may also exist for the residual base oils subcategory. However, only toxicity values (LL_0s) were provided without robust summaries. Robust summaries are needed before the data can be used to satisfy this endpoint. No data on the unrefined distillate base oils subcategory were provided in the test plan. Therefore, additional testing appears to be needed for this subcategory.

Invertebrates. Adequate data are available for the highly refined distillate base oils subcategory. No robust summaries or toxicity values were provided for the unrefined distillate base oils subcategory and only chronic toxicity values (LL_0s) without robust summaries were provided for the residual base oils subcategory. Therefore, the data are not adequate to satisfy this endpoint, and additional testing appears warranted for both of these subcategories.

Calculated log K_{ow} values of 4.9 to 7.7 for representative C15 components of base oils indicate a need for chronic aquatic invertebrate toxicity data for each of the subcategories. Adequate chronic data are available for the highly refined distillate base oils subcategory for the aquatic invertebrate chronic toxicity endpoint. Chronic toxicity values without robust summaries were submitted for two residual base oils. Robust summaries need to be prepared before the data can be used to support the chronic toxicity endpoint. Otherwise, additional testing may be warranted. No robust summaries or toxicity values were provided for any substance in the unrefined distillate base oils subcategory for the aquatic invertebrate chronic toxicity endpoint. Therefore, testing appears to be warranted to satisfy this endpoint.

Algae. Adequate data are available for the highly refined distillate base oils subcategory. A single toxicity value (LL_0) without robust summary was provided for one member of the residual base oils subcategory. A robust summary is needed before the data can be used to satisfy this endpoint. No data on the unrefined distillate base oils subcategory were provided in the test plan. Therefore, additional testing appears to be needed for this subcategory.

Specific Comments on the Robust Summaries

Health Effects

Repeated-dose toxicity. Unrefined distillate base oils: Information missing from the submitted 90-day dermal study of heavy vacuum gas oil includes method details, specific hematology, clinical chemistry and urinalysis parameters examined (unless there was an effect), identity of tissues weighed and microscopically examined, an adequate description of test substance, information on tested animals (*e.g.,* age and weight at the beginning of study) and statistical methods.

Highly refined distillate base oils: The submitter needs to provide information on tested animals (*e.g.,* age and weight at the beginning of study), identity of tissues microscopically examined, NOAEL/LOAEL, and statistical methods for the submitted 4-week inhalation study of three base oils (SRO, WTO, HBO).

Developmental toxicity. Unrefined distillate base oils: Details missing from the submitted dermal study on heavy vacuum gas oil include method details, an adequate description of test substance, information on tested animals (*e.g.,* age and weight at the beginning of study), NOAELs/LOAELs (maternal and fetal), and statistical methods.

Ecological Effects

Fish. Toxicity values without essential robust summary details were reported for several base oils.

Invertebrates. For the chronic studies, the summary indicated that "the analytical results provided no definitive evidence of stability of the test preparations." Analytical results, however, were not included in the summary. In addition, results of OECD-compliant 21-day tests in *Daphnia magna* were provided without robust summaries.

Algae. Toxicity values without essential robust summary details were reported for several base oils.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.